REMARKS/ARGUMENTS

Status of Claims

Upon entry of this paper, claims 7, 24-27, 33-34, 47, and 54 are canceled, claims 2, 4, 19-22, 29, 32, 43, 46, and 48-53 are amended, and new claims 55-59 are presented.

After entry of this paper, claims 2, 4, 18-22, 29, 32, 43, 46, 48-53, and 56-59 are pending. Applicants reserve the right to pursue one or more continuing applications to any canceled subject matter.

Support for Amendments

Independent claims 2 and 53 are amended exactly as suggested by the Examiner. Claims 19, 20, and 48-51 are amended to include the term "of" in place of "according to" as suggested by the Examiner. A similar amendment is made to claims 4, 21, 32, 43, and 52 for consistency. Claim 22 is amended to include the phrase "transformed with" in place of "comprising" as suggested by the Examiner. Support for the amendments can be found throughout the specification as filed.

Claims 21 and 22 are amended to include the phrase "of the *Pseudomonas* genus" which is the equivalent of the previous language in claim 54, i.e. the abbreviation "sp." is used when the species name is not specified.[1]

Amended claim 46 is an independent claim directed to a nucleic acid sequence comprising both the sacABCDEFGH operon and the sacIJ operon of SEQ ID NO:1. Amended claims 48 to 50 refer to the nucleic acid sequence of claim 46 wherein one of the genes in the sacIJ operon has been disrupted. Support can be found, for example, in Figure 6 which shows

[1] See, for example, the Wikipedia entry for "binomial nomenclature"

the compounds produced by some of the specific gene knock out mutants obtained by disruption of SEQ ID NO:1. For example, the disruption of sacI gene (SacI- mutant) leads to compounds P2, P14 and P19B. The disruption of sacJ gene (SacJ- mutant) leads to compounds P2, P14, P19B, P22A and P22B. Moreover, in pages 44 to 47 of the specification as filed, it is shown that the disruption of SacI gene with sacJ gene reconstitution leads to the isolation of the safracin compounds Safracin D and E. New claim 57 finds similar support.

Similarly, amended claim 51 refers to the nucleic acid sequence of claim 46 wherein the sacF and/or the sacG gene of the sacA-H operon has been disrupted. The specification provides support for a sacF- mutant and a sacG- mutant (see for example page 50, first and second paragraphs). The specification discloses that these mutants were not able to produce safracin, or either P2 or P14. However, the addition of chemically synthesized P2 to either one of the two mutants resulted in safracin production.

Support for amended method claim 29 and new method claims 56-59 can be found throughout the specification as filed and in the Examples. Specifically, claim 56 has support throughout the specification and for example in Fig. 1, or in page 14, first paragraph, wherein it is shown that there are two operons within SEQ ID NO:1, one being the eight gene operon sacABCDEFGH, the other being sacIJ. Moreover, in Fig. 6 it is shown that the wild type *P. fluorescens* A2-2 gene cluster (i.e., where none of the genes of the sacA-H or sacIJ operons has been disrupted) produces Safracin A and Safracin B, whereas the disruption of the SacI and/or SacJ genes results in the production of safracin analogues.

Support for claim 58, directed to a method of producing safracins using a sacF- mutant or a sacG- mutant, with the addition of P2 (3-hydroxy-5-methyl-O-methyltyrosine) in the culture medium, can be found in the first and second paragraphs of page 50.

Support for claim 59 can be found in Example 6 (pages 50 to 54), where the specification describes the production of Safracin A(OEt) and Safracin B(OEt) using a sacF-mutant, with the presence of the P2 derivative, P3 (3-hydroxy-5-methyl-O-ethyltyrosine), in the culture medium.

No new matter is entered.

Request for Rejoinder

Claim 29 and newly added claims 56-59 (based on canceled claims 33-34) are directed to methods of producing a safracin or safracin analogue, corresponding to Group IV of the Restriction Requirement of March 13, 2007. Upon an indication of allowable subject matter, Applicants respectfully request rejoinder of withdrawn claim 29 and newly added claims 56-59 as method claims that otherwise incorporate all of the limitations of the allowable subject matter.

Claim Objections

Claims 2, 4, 18-20, 32, 43, and 48-54 are objected to, but not rejected. Applicants understand that the claims are therefore considered by the Examiner to contain patentable subject matter. Applicants respectfully traverse the objections, and note that according to the MPEP, "[s]ome latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire" (MPEP 2173.02).

Nevertheless, in order to advance prosecution, Applicants have amended claims 2, 4, 19-22, 32, 43, and 48-53 as suggested by the Examiner. Specifically, independent claims 2 and 53 are amended exactly as suggested by the Examiner. Claims 19, 20, and 48-51 are amended to include the term "of" in place of "according to" as suggested by the Examiner. A similar amendment is made to claims 4, 21, 32, 43, and 52 for consistency. Claim 22 is amended to

include the phrase "transformed with" in place of "comprising" as suggested by the Examiner. Claim 26 is canceled, thereby rendering the objection moot.

With respect to the objection to claims 4, 43, and 52 for failing to further limit claim 2, Applicants respectfully traverse. Claim 2 presents (a), (b), (c), (d), and (e) in the alternative. Claim 4 corresponds to only (a) and part of (e). Claim 43 corresponds to (b). Claim 52 corresponds to (a). As such, Applicants understand that claims 4, 43, and 52 do in fact further limit claim 2.

With respect to the Examiner's suggestion to "spell out the species name of the organism" (OA, p. 4, lines 1-2) in claim 54, the claim is canceled, but claims 21 and 22 are amended to include the phrase "of the *Pseudomonas* genus" which is the equivalent of the previous language in claim 54. According to the standard nomenclature in the biological arts, the abbreviation "sp." is used when the species name is not specified.

Applicants respectfully request withdrawal of the objections. In addition, Applicants note that no change in scope is to be implied by the amendments, as they were in response to objections to form only.

Claim Rejections

Claims 7, 21-22, and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in such a way as to reasonably convey that the inventors at the time the application was filed had possession of the claimed invention. Applicants respectfully traverse. However, claims 7 and 24-27 are canceled, thereby rendering the rejection of those claims moot.

Claims 21 and 22 are amended to specify that the recombinant host cell is from the bacterial genus *Pseudomonas*. New claim 55 with similar language as claim 21 has been introduced. New claim 55 is directed to a recombinant host cell of the *Pseudomonas* genus transformed with a nucleic acid sequence of any one of claims 46, 48, 49, 50, or 51.

The use of a bacterial strain of the *Pseudomonas* genus as a host cell has been sufficiently described in the specification. As described in the specification, the safracin gene cluster of SEQ ID NO:1 has been isolated from *Pseudomonas fluorescens*. In addition, in Example 5 (page 49 through page 50), the heterologous expression of the safracin biosynthetic precursors genes for P2 (3-hydroxy-5-methyl-O-methyltyrosine) and P14 (3-methyl-O-methyltyrosine) production has been described. To overproduce P14 in a heterologous system (i.e., bacteria different from *Pseudomonas fluorescens*) sacE to sacH genes were cloned in a plasmid (pB7983). Similarly, to overproduce P2, sacD to sacH genes were cloned in a different plasmid (pB5H83). These plasmids were introduced separately in 3 different bacteria from the Pseudomonas genus: *P. fluorescens*, *P. putida* and *P. stutzeri* (see page 49, lines 20-23). It can be seen in the Examples that both P14 and P2 could be obtained when the various plasmids were expressed in a variety of bacteria. Accordingly, it is submitted that a recombinant host cell of the *Pseudomonas* genus containing a sequence of the invention has sufficient written description in the specification.

Applicants respectfully request withdrawal of the rejection.

Claims 46-47 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicants regard as their invention. Applicants respectfully traverse.

Amended claim 46 is an independent claim directed to a nucleic acid sequence comprising both the sacABCDEFGH operon and the sacIJ operon of SEQ ID NO:1. Amended

claims 48 to 51 refer to the nucleic acid sequence of claim 46 wherein one of the genes in the sacIJ operon has been disrupted. Support for the amendments is discussed above. For example, Figure 6 shows the compounds produced by some of the specific gene knock out mutants obtained by disruption of SEQ ID NO:1. The disruption of sacI gene (SacI- mutant) leads to compounds P2, P14 and P19B. The disruption of sacJ gene (SacJ- mutant) leads to compounds P2, P14, P19B, P22A and P22B. Alternatively, the specification at pages 44-47 shows that the disruption of SacI gene with sacJ gene reconstitution leads to the isolation of new safracin compounds Safracin D and E. The disruption of the sacF gene or the sacG gene is described on page 50 of the specification.

Applicants believe the previous rejection of claim 46 is moot, and respectfully request withdrawal of the rejection.

CONCLUSION

Based on the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejections and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. 13566.105008. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is

hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. 13566.105008.

Respectfully submitted,
King & Spalding, LLP

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By: /michael willis/
Kenneth H. Sonnenfeld / Michael A. Willis
Reg. No. 33,285 / Reg. No. 53,913

Customer Number 65989
Correspondence Address:
King & Spalding
1185 Avenue of the Americas
New York, NY 10036-4003
(212) 556-2100 Telephone
(212) 556-2222 Facsimile